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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 01/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,651	SCHOR ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/8/05, 8/18/05, and 11/10/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-9,29,60 and 61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *29* is/are allowed.

6)☒ Claim(s) *1,4,5,7-9,60 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/8/05* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: U.S.P.T.O. search report "us-09-581-651d-3.rni" (Result 2), pages 1-5.

DETAILED ACTION

1. The amendment filed November 10, 2005, is acknowledged and has been entered. Claims 2, 3, 10, 11, 26-42, 44, 47-51, 53, 56, and 58 have been canceled. Claims 1, 4, 5, 8, 9, and 29 have been amended. Claims 60 and 61 have been added.

2. The amendment filed August 18, 2005, is acknowledged and has been entered. Claims 6, 12, 13, 27, 57, and 59 have been canceled. Claims 1, 2, 4, 5, 8-11, 29, 36-38, 40-42, 47, 51, 56, and 58 have been amended.

3. The amendment filed June 8, 2005, is acknowledged and has been entered in part.

4. Claims 1, 4, 5, 7-9, 29, 60, and 61 are currently under prosecution.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

6. The requirement to elect a species of the invention of Group I set forth in section 8 of the Office action mailed May 3, 2002, has been withdrawn.

Drawings

7. Receipt of the replacement drawings filed June 8, 2005, is acknowledged. The drawing depicting Figure 3 is acceptable; however, the drawing depicting Figure 2 is not because in both instances "SEQ ID NO." is misspelled as "SEQ IS NO.".

Response to Amendment

8. At page 4 of the amendment filed November 10, 2005, Applicant has stated, "the Examiner agreed that a polynucleotide whose sequence is SEQ ID NO:2 is patentable".

Notably SEQ ID NO: 2 is an amino acid sequence, and contrary to any implication that a claim drawn to polypeptide comprising SEQ ID NO: 2 is patentable, it is not. During the interview the Examiner explained the reasons why such a claim is not patentable over the prior art of record, but noted that since the polynucleotide sequence of SEQ ID NO: 3 is free of the prior art, the claims could be amended to overcome the rejections that are currently of record over the prior art. As explained in the Interview Summary mailed November 9, 2005, the Examiner proposed entry of an examiner's amendment, which would place this application in condition for allowance, but Applicant's representatives opted not to authorize its entry in favor of filing a supplemental amendment.

Grounds of Objection and Rejection Withdrawn

9. Without acquiescing to Applicant's arguments, the rejections of claims under 35 U.S.C. §§ 102 or 103, as being anticipated by Grey et al., as evidenced by Schor et al., or obvious Grey et al., as evidenced by Schor et al., in view of Bendig, for the reasons set forth in sections 25 and 29 of the preceding Office action have been withdrawn in favor of the new grounds of rejection set forth below.

Otherwise, unless specifically reiterated below, Applicant's amendment and/or arguments filed June 8, 2005, August 18, 2005, and/or November 10, 2005, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed December 7, 2004.

Grounds of Objection and Rejection Maintained

Drawings

10. The objection to the drawing sheet setting forth Figure 2 (Part 2), because "SEQ ID NO." is misspelled as "SEQ IS NO." in both instances, is maintained. As noted above, although a replacement sheet was filed June 8, 2005, this issue has not been resolved. Appropriate correction is required.

Specification

11. The objection to the specification, because the use of improperly demarcated trademarks, is maintained. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Although it appears Applicant has made a *bona fide* attempt to correct this issue, another example of an improperly demarcated trademark is found at page 47, line 19, of the substitute specification filed June 8, 2005, namely pBlueScript™.

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

Claim Rejections - 35 USC § 112

12. The rejection of claims 9 and 61 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained.

Claims 9 and 61 are indefinite because the claims recite a limitation that the polypeptide has "the migration stimulating factor activity of the polypeptide having the amino acid sequence of SEQ ID NO: 2". Although claims 9 and 61 depend directly or directly from claim 1, which defines the migration stimulation activity of a polypeptide having the amino acid sequence of SEQ ID NO: 2 as "[the] ability to stimulate adult skin fibroblast migration into collagen gel", claims 9 and 61 are not necessarily so limited, since claims 9 and 61 are only required to be processes comprising culturing a host cell comprising a polynucleotide according to claim 1. In other words, although the host cells cultured in the claimed processes comprise a polynucleotide according to claim 1, the recitation does not limit the method to a process for making a polypeptide having

"[the] ability to stimulate adult skin fibroblast migration into collagen gel", because the polypeptide made according to the claimed process is not necessarily a polypeptide encoded by a polynucleotide according to claim 1. Furthermore, as explained in the preceding Office action, the specification does not clearly and particularly define what functional activity or activities constitute "the migration stimulating factor activity" of the polypeptide of SEQ ID NO: 2. Accordingly, the metes and bounds of the subject matter that Applicant regards as the invention cannot be ascertained with the requisite degree of particularity and clarity, so as to permit the skilled artisan to determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

13. The rejection of claims 1, 7, 8, 9, 60, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

At pages 11 and 12 of the amendment filed June 8, 2005, and at pages 11 and 12 of the amendment filed August 18, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The claims are directed to nucleic acid molecules encoding a genus of structurally and functionally variable polypeptides. More specifically the claims are directed to nucleic acid molecules having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Moreover, the claims are not limited to nucleic acid molecules comprising the disclosed polynucleotide

sequences that encode a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, but rather encompass nucleic acid molecules encoding variants of this polypeptide.

Although the members of the claimed genus of nucleic acid molecules necessarily comprise a polynucleotide sequence that is at least 90% homologous to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, the members are not required to have any particular degree of identity to the disclosed polynucleotide sequence of SEQ ID NO: 3, which encodes the amino acid sequence of SEQ ID NO: 2. Accordingly, the claims are directed to a genus of nucleic acid molecules that vary substantially in structure.

Although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, which elicits antibodies that recognize "migration stimulation factor", but not fibronectin, the polypeptides themselves are not required to have any degree of structural homology (i.e., similarity) or identity to the amino acid sequence of SEQ ID NO: 2. Accordingly, the claims are directed to a genus of nucleic acid molecules that vary substantially in structure and encode polypeptides, which although commonly having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and commonly having the ability to elicit antibodies that recognize "migration stimulation factor", but not fibronectin, vary substantially in structure.

Although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, the members of the genus cannot be immediately envisioned, recognized or distinguished from other nucleic acid molecules encoding other proteins. The specification describes only one polypeptide encoded by the claimed genus of nucleic acid molecules, namely the polypeptide of SEQ ID NO: 2. Neither the nucleic acid molecules encoding the polypeptide of SEQ ID NO: 2 (e.g., the nucleic acid molecule of SEQ ID NO: 3) nor the polypeptide itself are described in sufficient and detailed manner, so as to reasonably be considered

representative of the genus, as a whole, since there is no disclosure of a particularly identifying (i.e., substantial) structural feature shared by at least most of the polypeptides encoded by the claimed nucleic acid molecules that correlates with the polypeptides' ability to stimulate adult skin fibroblasts migration into collagen gel, which is at least 30% of the same activity of a polypeptide comprising SEQ ID NO: 2.

Although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides that elicit antibodies that recognize "migration stimulation factor", but not fibronectin, the members of the genus cannot be immediately envisioned, recognized or distinguished from other nucleic acid molecules encoding other proteins. Again, the specification describes only one polypeptide encoded by the claimed genus of nucleic acid molecules, namely the polypeptide of SEQ ID NO: 2. Neither the nucleic acid molecules encoding the polypeptide of SEQ ID NO: 2 (e.g., the nucleic acid molecule of SEQ ID NO: 3) nor the polypeptide itself are not described in sufficient and detailed manner, so as to reasonably be considered representative of the genus, as a whole, since there is no disclosure of the presence of a shared, particularly identifying structural feature, which in this case is necessarily a common antigenic determinant (i.e., the epitope to which an antibody that recognizes the protein encoded by the claimed nucleic acid molecule, which is not presented by fibronectin), that correlates with their shared "migration stimulation factor activity". Moreover, the recitation of a limitation requiring the polypeptide encoded by the members of the claimed genus of nucleic acid molecules to elicit an antibody that binds specifically to "migration stimulation factor", but not fibronectin, would not reasonably convey to the skilled artisan that, as of the filing date sought, the Applicant had possession of the claimed invention, because the recitation does not provide a description of any uniquely defining or identifying feature that is common to at least a substantial number of members of the claimed genus, which would descriptively set the genus apart from just any polypeptide encoded by a nucleic acid molecule having the required similarity (i.e., at least 90% homology) to the reference amino acid sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2.

With particular regard to claims 9 and 61, the claims are directed to methods for making a polypeptide having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, said methods comprising culturing a cell comprising a polynucleotide according to claim 1, but the polypeptide produced by the claimed methods is not necessarily a polypeptide encoded by the polynucleotide according to claim 1. Thus, claims 9 and 61 are directed to methods for making structurally variant polypeptides encoded by any nucleic acid molecule of which said host cell is comprised, which commonly have at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2.

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Insofar as the claims are directed to structurally varying nucleic acid molecules encoding polypeptides that differ both structurally and functionally from the disclosed polypeptides comprising the amino acid sequence of SEQ ID NO: 2, the specification fails to describe the claimed invention with the requisite detail and particularity that is necessary to satisfy the written description requirement set forth under 35 U.S.C. 112, first paragraph. "[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes the genus of nucleic acid molecules. A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

Even whilst the nucleic acid molecules encompassed by the claims encode polypeptides that have recognizable functions, it is again aptly noted that the Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability stimulate adult skin fibroblasts migration into collagen gel, which is at least 30% of the same activity of a polypeptide comprising SEQ

ID NO: 2, and to elicit an antibody that cross-reacts with the polypeptide of SEQ ID NO: 2 without binding fibronectin, does not provide an adequate written description of the genus. See *The Reagents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). The Court indicated that while applicants are not required to disclose every species encompassed by a genus; the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

In addition, although the skilled artisan could potentially screen candidate nucleic acid molecules to identify those that encode polypeptides that are encompassed by the claims, which have those recognizable functions, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Finally, Applicant is again reminded that Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the

invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Because the claims encompass a genus of nucleic acid molecules encoding polypeptides, which vary both structurally and functionally, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

Thus, while the disclosure might be considered to provide *ipsis verbis* support for the claimed invention, the Federal Circuit has explained that *in ipsis verbis* support does not *per se* establish compliance with the written description requirement:

> Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *See also:* University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 1892 (CA FC 2004).

14. The rejection of claims 1, 7, 8, 9, 60, and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** an isolated, recombinant nucleic acid molecule encoding a polypeptide

comprising the amino acid sequence of SEQ ID NO: 2, an isolated, recombinant nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 3 from the nucleotide at position 57 through the nucleotide at position 1982, a isolated replicable vector comprising any of said polynucleotide sequences, an isolated host cell comprising said vector, and a method for producing said polypeptide by a process comprising culturing said host cell and isolating said polypeptide, or any nucleic acid molecule taught by the prior art, **does not reasonably provide enablement for making and using** a nucleic acid molecule having a polynucleotide sequence that is at least 90% homologous to a recombinant polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which stimulates adult skin fibroblasts migration into collagen gel with at least 30% of the same activity of a polypeptide comprising SEQ ID NO: 2 and elicits an antibody that cross-reacts with the polypeptide of SEQ ID NO: 2 without binding fibronectin, a replicable vector comprising said polynucleotide sequence, an isolated host cell comprising said polynucleotide sequence, or a method for producing a polypeptide that stimulates adult skin fibroblasts migration into collagen gel with at least 30% of that activity of a polypeptide comprising SEQ ID NO: 2, said method comprising culturing a host cell comprising said polynucleotide sequence and isolating the polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/or the invention commensurate in scope with these claims.

At pages 11 and 12 of the amendment filed June 8, 2005, and at pages 11 and 12 of the amendment filed August 18, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to

> practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

As explained above in the rejection of claims under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, the claims are directed to nucleic acid molecules of considerable structural variability, which encode polypeptides that differ markedly, both in structure and function. As explained in the preceding Office action, the state of the art, the level of skill in the art, and the unpredictability in the art are such that absent guidance, direction, and exemplification that is more reasonably commensurate in scope with the scope of the claims, the skilled artisan, at the time the application was filed, could not without undue and/or unreasonable experimentation make and/or use the claimed invention. This position is supported by references cited in the preceding Office action, including Skolnick et al. (of record), Burgess et al. (of record), and Lazar et al. (of record).

The claims are directed to nucleic acid molecules that encode variants of the disclosed polypeptide of SEQ ID NO: 2, which have or retain at least 30% of the ability of the polypeptide of SEQ ID NO: 2 to stimulate adult skin fibroblasts to migrate into collagen gel, as measured using an assay described by Picardo et al. (of record).

However, as explained previously, the specification fails to teach which amino acid residues of SEQ ID NO: 2 are critical to this particular function of the polypeptide of SEQ ID NO: 2. Moreover, the specification fails to teach by which other amino acids such critical residues can be replaced without loss of activity. Absent such necessary guidance and direction, because the skilled artisan cannot reliably and accurately predict the effects of amino acid substitutions, deletions, or insertions in the amino acid sequence of a given polypeptide, the disclosure would not be sufficient to have enabled the skilled artisan at the time the application was filed to make, and therefore use, the claimed invention.

Furthermore, there is no factual evidence of record that reasonably supports any assertion that the mere presence of a common antigenic determinant correlates with, or determines a common "migration stimulation factor activity" of any polypeptide encoded by nucleic acid molecules having sequences that are at least 90% homologous (i.e., similar to) a nucleic acid molecule encoding a polypeptide comprising SEQ ID NO: 2. Therefore, although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides that elicit antibodies that recognize "migration stimulation factor", but not fibronectin, it is submitted that the members of the genus cannot be distinguished from other nucleic acid molecules encoding other proteins simply by using the encoded polypeptide to elicit antibodies and then determining if the antibodies bind the polypeptide without binding fibronectin. As such, the requirement that the claimed nucleic acid molecules encode antigenically related polypeptides does not remedy the insufficiency of the guidance and direction that would otherwise, if present and sufficient, enable the skilled artisan to make the claimed nucleic acid molecules encoding variants of the polypeptide of SEQ ID NO: 2.

Echoing this fact, Takada et al. (*Mol. Endocrinol.* 2000; **14** (5): 733-740) teaches that the lack of predictability in the art remains, despite technological advances and a better understanding of the structure-function relationship; see entire document (e.g., the abstract). Takada et al. teaches their work illustrates that a single amino acid change may be sufficient to cause the acquisition of a new ligand binding specificity as well as to suppress recognition of a previous ligand, extending observations by others

who showed that changes in one or several amino acids can result in marked alterations in activity and function of nuclear receptors (page 738, column 1). Notably, Takada et al. teaches that the functional consequence of amino acid substitution may be rather subtle, since the variants of the receptors were still able to bind to the promoter of the reporter construct and activate transcription in the presence of some ligands but not others; see, e.g., page 739, Figure 5. Takada et al. teaches the difference in ligand binding specificity caused by the amino acid changes results in the variants having the activity of different member of the family of proteins; see, e.g., the abstract. Thus, Takada et al. discloses that seemingly subtle differences resulting from amino acid differences, such as changes in ligand binding specificity, may cause variants of a protein to have a function that differs markedly from that of the protein. Accordingly, depending upon the assay used to assess the activity of the proteins and its variants, the effects of amino acid sequence variation may not be immediately recognized or appreciated, since the variants may appear to function normally otherwise, but in actuality have substantially different functions.

Even more recently, Guo et al. (*Proc. Natl. Acad. Sci. USA.* 2004 Jun 22; **101** (25): 9205-9210) have calculated the probability that a random amino acid substitution, such as that which might occur naturally during aging or as a consequence of evolution or disease, will cause inactivation of a protein; see entire document (e.g., the abstract). Guo et al. reports this probability was found to be 34% ± 6% (abstract); that is, 34% of random mutations in the sequence of a protein are predicted to cause the inactivation of the protein. Guo et al. observed that various residues are differentially sensitive to substitutions, but the tolerance of the entire protein to random change can be defined by the probability that any given random amino acid substitution will inactivate the protein (i.e., the so-called "*x* factor") (page 9209, column 2). Not surprisingly, evolutionarily conserved residues showed low substitutability indices (abstract).

Thus, Lazar et al. (of record), for example, shows that even a single, conservative amino acid change can cause substantial changes in the activity of a protein, so it is evident that the skilled artisan cannot predict the functional consequences of amino acid substitutions and must determine those consequences

empirically; and since Guo et al. (*supra*) shows that amino acid substitutions are remarkably likely to cause inactivation of the protein, it is even more apparent that the functional consequences of the amino acid differences must be ascertained before any given variant of a protein can be used in the same manner in which the protein having a known function is used.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), there is a preponderance of factual evidence of record that indicates the disclosure would not be sufficient to have enabled the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 102

15. The rejection of claims 1, 7-9, 60, and 61 under 35 U.S.C. 102(b), as being anticipated by WO 94/16085 A2 (of record), is maintained.

At page 14 of the amendment filed June 8, 2005, and at page 14 of the amendment filed August 18, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but are not found persuasive for the following reasons:

Claim 1 is drawn to a recombinant polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or alternatively to a polynucleotide having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Claim 7 is drawn to a replicable vector comprising a recombinant polynucleotide according to claim 1. Claims 8 and 60 are drawn to an isolated host cell comprising a recombinant polynucleotide according to claim 1, or a replicable vector according to claim 7, respectively. Claims 9 and 61 are drawn to methods for making a polypeptide having at least 30% of the "migration

stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, said methods comprising culturing a host cell comprising a polynucleotide according to claim 1, or a host cell according to claim 60, respectively.

"Homology" is defined, for example, by Merriam-Webster Online Dictionary, which available on the Internet at http://www.merriam-webster.com/, as "similarity of nucleotide or amino-acid sequence in nucleic acids, peptides, or proteins" (copyright 2005 by Merriam-Webster, Incorporated). Homology or similarity of nucleic acid sequences may be evaluated by relatively subjective criterion, or it may be objectively measured using any of wide variety of differing criterion.

Accordingly, the claims are not limited to nucleic acid molecules comprising a polynucleotide sequence that is at least 90% identical to any particular polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2, such as the polynucleotide sequence of SEQ ID NO: 3. Rather the claims are directed to a genus of structurally varying nucleic acid molecules that are somehow determined to be 90% homologous (i.e., similar) to a polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2

WO 94/16085 A2 (Irani) teaches an isolated, recombinant nucleic acid molecule comprising a polynucleotide that encodes a polypeptide that is 97.1% identical to amino acid sequence of SEQ ID NO: 2; see entire document (e.g., SEQ ID NO: 2). Irani teaches the polypeptide encoded by the disclosed nucleic acid molecule is produced by a process comprising culturing a host cell comprising a replicable vector comprising a polynucleotide sequence encoding the polypeptide and purifying the polypeptide; see, e.g., page 8, line 27, through page 15, line 12.

When compared to the polynucleotide sequence of SEQ ID NO: 3, which is the disclosed polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, the polynucleotide sequence disclosed by the prior art (i.e., SEQ ID NO: 1) has a "best local similarity" of 97.1%; see the attached copy of part of the U.S.P.T.O. search report "us-09-581-651d-3.rni" (Result 3), which was generated by searching the Office's "Issued Patents NA" database using SEQ ID NO: 3 as a query.

Although Irani et al. does not expressly teach the polypeptide encoded by the disclosed nucleic acid molecule has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and elicits antibodies that recognize "migration stimulation factor" but not fibronectin, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed polynucleotide, replicable vector, and host cell, or for examining and comparing Applicant's process with process of the prior art to establish that the claimed method for making a polypeptide and the methods of the prior art produce distinguishable products.

Given the fact that the nucleic acid molecule disclosed by the prior art encodes a polypeptide having an amino acid sequence that is 94.8% identical to amino acid sequence of SEQ ID NO: 2, the claimed products and processes are deemed the same as those disclosed by the prior art, absent a showing of any difference.

In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products and processes are different than those taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

New Grounds of Rejection

Claim Rejections - 35 USC § 101

16. Claims 1, 4, 5, and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 4, and 5 are specifically drawn to "recombinant" polynucleotides, whereas claims 7 is drawn to a replicable vector comprising a polynucleotide as defined in claim 1.

The Merriam-Webster's Online Dictionary, 10th Edition (copyright © 2005 by Merriam-Webster, Inc.), which is available on the Internet at http://www.m-w.com/, defines the term "recombinant" as "relating to or containing recombinant DNA".

Because claims 1, 4, 5, and 7 are drawn to recombinant polynucleotides and replicable vectors comprising such polynucleotides, *which are not necessarily isolated*, the claims are broadly but reasonably interpreted to encompass nucleic acid molecules and replicable vectors that are present in cells, which are not isolated but rather comprised *within* an organism, including a human. Support for this interpretation of the claims is found throughout the specification; for example, at page 44, lines 10 and 11, the specification, as originally filed, contemplates the use of gene therapy to administer to patients (i.e., humans) the claimed replicable vector comprising the claimed nucleic acid sequence encoding the disclosed polynucleotide. Host cells comprised within the patient are "transformed" or "transfected" with the recombinant nucleic acid molecules encoding the polypeptide, or replicable vectors (e.g., retroviral vectors) comprising the polynucleotide sequences of such nucleic acid molecules; see, e.g., page 12, line 23, through page 13, line 28. Accordingly, the claims encompass such recombinant nucleic acid molecules and replicable vectors, which are comprised within the cells of treated patients.

MPEP § 2105 [R-1] states:

> If the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter.

With further regard to claims 1, 4, and 5, it is aptly noted the Merriam-Webster's Online Dictionary, 10th Edition (copyright © 2005 by Merriam-Webster, Inc.) provides an alternative definition of the "recombinant", namely "relating to or exhibiting genetic recombination". Given this definition, it is not apparent that the claimed subject matter is distinguishable from a naturally occurring polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, such as the messenger RNA (mRNA) molecule of which human cells are naturally comprised, which encodes the polypeptide of SEQ ID NO: 2. Accordingly, giving the claims the broadest, reasonable interpretation that is consistent with both the specification and that which the skilled artisan would have, the claims are drawn to non-statutory subject matter (i.e., a naturally occurring product).

Moreover, claim 1 is drawn to a recombinant polynucleotide encoding a polypeptide, or alternatively to a polynucleotide, albeit not necessarily recombinant or isolated having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 (e.g., a sequence at least 90% homologous to SEQ ID NO: 3) and encoding a polypeptide that has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin.

These issues can be remedied by amending claims 1, 4, 5, and 7 to recite the limitation "isolated" before "recombinant polynucleotide" or "replicable vector".

Claim Rejections - 35 USC § 112

17. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn a polynucleotide having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the migration stimulation factor activity of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Claims 7-9, 60, and 61 depend from claim 1.

The claims are indefinite because claim 1 uses the term "migration stimulation factor" to define the polypeptide by which antibodies elicited by the claimed polypeptide are recognized without also recognizing fibronectin. The use of laboratory designations only to identify a particular polypeptide renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct polypeptides. In the absence of clear and particular identification of the polypeptide to which the claims are directed, the metes and bounds of the subject matter that Applicant regards as the invention are sufficiently delineated, so as to permit the skilled

artisan to determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

This issue may be remedied by amending claim 1 to reference to the amino acid sequence of "migration stimulation factor" to which the claims are directed because the amino acid sequence of a polypeptide is a unique identifier that unambiguously defines a given polypeptide.

18. Claims 1, 4, 5, and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** an *isolated*, recombinant nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, an *isolated*, recombinant nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 3, and an *isolated* replicable vector comprising the polynucleotide sequence of any of the aforementioned nucleic acid molecules, **does not reasonably provide enablement for making and using** any such *non-isolated* nucleic acid molecules or replicable vectors encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As explained in the above rejection of claims 1, 4, 5, and 7 under 35 U.S.C. 101, the claims encompass the polynucleotides according to claim 1 or the replicable vectors (e.g., a recombinant retrovirus) according to claim 7, which have been introduced into cells comprised within an organism, including humans that are treated with such polynucleotides and replicable vectors. Again, support for this interpretation of the claims is found throughout the specification, as originally filed (e.g., page 12, line 23, through page 13, line 28; page 42, lines 6-8; and page 44, lines 10 and 11).

However, as explained in section 21 of the preceding Office action with regard to claim 8, the amount of guidance, direction, and exemplification set forth in the specification would not be sufficient to enable the skilled artisan to make and use the claimed invention without undue and/or unreasonable experimentation. This position was supported by the teachings of Houdebine (of record), Verma et al. (of record)

Amalfitano et al. (of record), Pandha et al. (of record), and the memorandum dated January 14, 2003, by Dr. Patterson of the U.S. Department of Health and Human Services. This ground of rejection set forth in the preceding Office action is herein reiterated with respect to claims 1, 4, 5, and 7, as these claims are broadly but reasonably interpreted to encompass polynucleotides and replicable vectors comprising polynucleotide sequences encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which have been introduced into cells of which animals, including humans are comprised.

Notably it would be remedial to amend claims 1, 4, 5, and 7 to recite the limitation "isolated" before "recombinant polynucleotide" or "replicable vector".

19. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "new matter" rejection.

Claim 1 recites, "wherein migration stimulation factor activity refers to ability to stimulate adult skin fibroblast migration into collagen gel".

At page 5 of the amendment filed November 11, 2005, Applicant has asserted that written support for the language of the claim 1 is found throughout the specification but, in particular, at page 9.

Although the specification, as originally filed, describes assessing the activity of members of a genus of "MSF polypeptides" in "bioassays based on its stimulation of adult skin fibroblast migration, for example, as in Picardo *et al* (1991) *The Lancet* 337, 130-133" (page 10, lines 1-6), this disclosure is insufficient to provide proper written support for defining the migration stimulation factor activity of the genus of polypeptides to which the claims are directed as "[the] ability to stimulate adult skin fibroblast migration **into collagen gel**" (emphasis added).

Furthermore, although the specification cites Picardo et al. as describing such a biosassay, MPEP § 608.01(p) does not provide for the incorporation by reference of essential material by reference to non-patent publications. "Essential material" is defined as "that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112)". The bioassay described by Picardo et al. is essential information because claim 1 presently recites, "wherein migration stimulation factor activity refers to ability to stimulate adult skin fibroblast migration into collagen gel", and thus the disclosure of Picardo et al. describing such a bioassay is necessary to describe, if not enable, the claimed invention.

It is suggested this issue may be remedied by incorporating relevant portions of the disclosure of Picardo et al. (of record), which provide sufficient written support for the present claim language. Applicant should do so by amending the specification to include this material incorporated by reference to Picardo et al., and the amendment must be accompanied by an affidavit or declaration executed by Applicant, or a practitioner representing Applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

21. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,830,700 A, as evidenced by the attached copy of part of the U.S.P.T.O. search report "us-09-581-651d-3.rni" (i.e., Result 2), which was generated by searching the Office's "Issued Patents NA" database using SEQ ID NO: 3 as a query.

Claim 1 is drawn to a recombinant polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or alternatively to a polynucleotide having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Claim 7 is drawn to a replicable vector comprising a recombinant polynucleotide according to claim 1. Claims 8 and 60 are drawn to an isolated host cell comprising a recombinant polynucleotide according to claim 1, or a replicable vector according to claim 7, respectively. Claims 9 and 61 are drawn to methods for making a polypeptide having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, said methods comprising culturing a host cell comprising a polynucleotide according to claim 1, or a host cell according to claim 60, respectively.

"Homology" is defined, for example, by Merriam-Webster Online Dictionary, which available on the Internet at http://www.merriam-webster.com/, as "similarity of nucleotide or amino-acid sequence in nucleic acids, peptides, or proteins" (copyright 2005 by Merriam-Webster, Incorporated). Homology or similarity of nucleic acid sequences may be evaluated by relatively subjective criterion, or it may be objectively measured using any of wide variety of differing criterion.

Accordingly, the claims are not limited to nucleic acid molecules comprising a polynucleotide sequence that is at least 90% identical to any particular polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2, such as the polynucleotide sequence of SEQ ID NO: 3. Rather the claims are directed to a genus of structurally varying nucleic acid molecules that are somehow determined to be 90%

homologous (i.e., similar) to a polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2

U.S. Patent No. 5,830,700 A (Irani) teaches an isolated, recombinant nucleic acid molecule comprising a polynucleotide that encodes a polypeptide that is 97.1% identical to amino acid sequence of SEQ ID NO: 2; see entire document (e.g., SEQ ID NO: 1). Irani teaches the polypeptide encoded by the disclosed nucleic acid molecule is produced by a process comprising culturing a host cell comprising a replicable vector comprising a polynucleotide sequence encoding the polypeptide and purifying the polypeptide; see, e.g., column 5, line 54, through column 8, line 44.

When compared to the polynucleotide sequence of SEQ ID NO: 3, which is the disclosed polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, the polynucleotide sequence disclosed by the prior art has a "best local similarity" of 97.1%; see the attached copy of part of the U.S.P.T.O. search report "us-09-581-651d-3.rni" (Result 2), which was generated by searching the Office's "Issued Patents NA" database using SEQ ID NO: 3 as a query.

Although Irani et al. does not expressly teach the polypeptide encoded by the disclosed nucleic acid molecule has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and elicits antibodies that recognize "migration stimulation factor" but not fibronectin, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed polynucleotide, replicable vector, and host cell, or for examining and comparing Applicant's process with process of the prior art to establish that the claimed method for making a polypeptide and the methods of the prior art produce distinguishable products.

Given the fact that the nucleic acid molecule disclosed by the prior art encodes a polypeptide having an amino acid sequence that is 94.8% identical to amino acid sequence of SEQ ID NO: 2, the claimed products and processes are deemed the same as those disclosed by the prior art, absent a showing of any difference.

In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products and processes are different than those taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

22. Claim 9 is rejected under 35 U.S.C. 102(b), as being anticipated by Grey et al. (of record), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751.

Claim 9 is drawn to a method for making a polypeptide having at least 30% of the migration stimulation activity of the polypeptide having the amino acid sequence of SEQ ID NO: 2, said method comprising culturing a host cell comprising a polynucleotide according to claim 1.

As explained in the below rejection of claim 1 under 35 U.S.C. § 101, claim 1 encompasses a naturally occurring nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, such as the gene or messenger RNA (mRNA) transcribed from the gene encoding the polypeptide, which is expressed naturally in certain cells. As evidenced by Schor et al., GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, Grey et al. teaches culturing cells comprising such naturally occurring nucleic acid molecules encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2; see, e.g., page 2438, column 2, through page 2439, column 1. Grey et al. teaches isolating the polypeptide expressed by the cultured cells; see, e.g., page 2439, columns 1 and 2. Because the polypeptide comprises the amino acid sequence of SEQ ID NO: 2, it is expected to have at least 30% of the migration stimulation activity of the polypeptide having the amino acid sequence of SEQ ID NO: 2.

For further clarity, a polynucleotide according to claim 1 is not isolated, nor is it necessarily recombinant. Claim 1 is alternatively drawn a polynucleotide, albeit not necessarily recombinant, having a sequence with at least 90% homology to a

polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the migration stimulation factor activity of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Nevertheless, even if claim 1 is limited to a "recombinant" polynucleotide, as explained in greater depth and detail below in the rejection of claim 1 under 35 U.S.C. § 101, a "recombinant" polynucleotide cannot be distinguished from a naturally occurring nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, such as the gene or mRNA transcribed from the gene encoding the polypeptide, which are found in the cells such as those disclosed by Grey et al.

In traversing the ground of rejection of claims under 35 U.S.C. § 102, as being anticipated by Grey et al., as evidenced by Schor et al. (*Cancer Res.* 2003 Dec; **63** (24): 8827-8836) (of record), which was set forth in the preceding Office action, Applicant argued that there is no evidence that Grey et al. necessarily discloses a protein having the amino acid sequence of SEQ ID NO: 2; see, e.g., page 13 of the amendment filed June 8, 2005. Moreover, Applicant contended the polypeptide disclosed by Grey et al. may not be the disclosed polypeptide having the amino acid sequence of SEQ ID NO: 2, since it could be another polypeptide, such as the polypeptide disclosed by database EMBL Accession No. AJ535086, which comprises 15 amino acids not present in the amino acid sequence of SEQ ID NO: 2, as depicted in Figure 2. Applicant stated the amino acid sequence encoded by the polynucleotide sequence of EMBL Accession No. AJ535086 is 657 amino acids in length, whereas the amino acid sequence depicted in Figure 2 (i.e., SEQ ID NO: 2) is only 642 amino acids.

Without acquiescing to Applicant's arguments, it is herein noted that Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379) teaches the polynucleotide sequence of a complementary DNA molecule encoding "MSF", the 70 kDa polypeptide first purified by Grey et al., was submitted to the database EMBL under the accession number AJ276395; see entire document (e.g., page 376, columns 1 and 2). According to EMBL/GenBank™ Accession No. AJ276395, the amino acid sequence that is encoded by the disclosed polynucleotide sequence is reported in database UniProtKB/Swiss-

Prot™ under the accession number P02751. According to UniProtKB/Swiss-Prot™ Accession No. P02751, the amino acid sequence of the alternative splice form-2, designated "MSF FN-70" and described by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379)) is 642 amino acids.

The Examiner cannot account for the disparity between the amino acid sequence reported by Schor et al. as EMBL/GenBank™ Accession No. AJ276395 (i.e., the 642 amino acid sequence) and amino acid sequence, also reported by Schor et al., of EMBL Accession No. AJ535086 (i.e., the 657 amino acid sequence). Nevertheless, as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379) and corresponding disclosures in the databases, it appears that the 70 kDa polypeptide produced by the fibroblasts cultured by Grey et al. is the polypeptide of SEQ ID NO: 2.

Again, in the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products and processes are different than those taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

Claim Rejections - 35 USC § 103

23. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grey et al. (of record), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, in view of Bendig (of record).

Grey et al. and Bendig teach that which is set forth in section 29 of the preceding Office action.

As explained in the above rejection of claim 9 under 35 U.S.C. 102(b), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, the 70 kDa polypeptide designated "migration stimulation factor (MSF)", which was isolated from cultured fibroblasts by Grey et al., is the polypeptide of SEQ ID NO: 2.

Grey et al. teaches, "[o]ur current efforts are directed toward cloning the gene for MSF and obtaining its complete sequence" (page 2441, column 1).

As explained in the preceding Office action, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made to have cloned a nucleic acid molecule encoding the polypeptide disclosed by Grey et al. because Grey et al. teaches efforts are underway to do exactly that, and Bendig teaches the methodology necessary to do so was well within the skill of the artisan of ordinary skill at the time the invention was made. Accordingly, as also explained in the preceding Office action, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to produce a host cell comprising a vector comprising the cloned polynucleotide sequence encoding the polypeptide by recombinant DNA technology in accordance with the teachings reviewed by Bendig and then culture the host cells and isolate the polypeptide produced by the host cells in the culture. Therefore, among other reasons, one ordinarily skilled in the art at the time of the invention would have been motivated to do so to facilitate production of the polypeptide by recombinant means.

Conclusion

24. Claim 29 is allowed; no other claim is allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
January 17, 2006

Alternative Splicing of entry: P02751

Splice Isoform: 2

Isoform description	
Name	**2**
Synonyms	MSF-FN70, Migration stimulation factor FN70
Isoform ID	P02751-2
Features which should be applied to build the isoform sequence: VSP_003255, VSP_003256, VSP_003257	

Sequence information

Length: **642 AA**

```
        10         20         30         40         50         60
         |          |          |          |          |          |
MLRGPGPGLL LLAVQCLGTA VPSTGASKSK RQAQQMVQPQ SPVAVSQSKP GCYDNGKHYQ

        70         80         90        100        110        120
         |          |          |          |          |          |
INQQWERTYL GNALVCTCYG GSRGFNCESK PEAEETCFDK YTGNTYRVGD TYERPKDSMI

       130        140        150        160        170        180
         |          |          |          |          |          |
WDCTCIGAGR GRISCTIANR CHEGGQSYKI GDTWRRPHET GGYMLECVCL GNGKGEWTCK

       190        200        210        220        230        240
         |          |          |          |          |          |
PIAEKCFDHA AGTSYVVGET WEKPYQGWMM VDCTCLGEGS GRITCTSRNR CNDQDTRTSY

       250        260        270        280        290        300
         |          |          |          |          |          |
RIGDTWSKKD NRGNLLQCIC TGNGRGEWKC ERHTSVQTTS SGSGPFTDVR AAVYQPQPHP

       310        320        330        340        350        360
         |          |          |          |          |          |
QPPPYGHCVT DSGVVYSVGM QWLKTQGNKQ MLCTCLGNGV SCQETAVTQT YGGNSNGEPC
```

```
       370         380         390         400         410         420
        |           |           |           |           |           |
VLPFTYNDRT DSTTSNYEQD QKYSFCTDHT VLVQTQGGNS NGALCHFPFL YNNHNYTDCT

       430         440         450         460         470         480
        |           |           |           |           |           |
SEGRRDNMKW CGTTQNYDAD QKFGFCPMAA HEEICTTNEG VMYRIGDQWD KQHDMGHMMR

       490         500         510         520         530         540
        |           |           |           |           |           |
CTCVGNGRGE WTCIAYSQLR DQCIVDDITY NVNDTFHKRH EEGHMLNCTC FGQGRGRWKC

       550         560         570         580         590         600
        |           |           |           |           |           |
DPVDQCQDSE TGTFYQIGDS WEKYVHGVRY QCYCYGRGIG EWHCQPLQTY PSSSGPVEVF

       610         620         630         640
        |           |           |           |
ITETPSQPNS HPIQWNAPQP SHISKYILRW RPVSIPPRNL GY
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GenCore version 5.1.6

OM nucleic - nucleic search, using sw model

Run on: November 10, 2005, 22:35:24 ; Search time 367 Seconds
(without alignments)
9572.442 Million cell updates/sec

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Scoring table: IDENTITY_NUC
Gapop 10.0 , Gapext 1.0

Searched: 1202784 seqs, 818138359 residues

Total number of hits satisfying chosen parameters: 2405568

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Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

	Result No.	Score	% Query Match	Length	DB	ID	Description
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	2	1826.8	85.1	7803	2	US-08-551-356-1	Sequence 1, Appli
	3	1826.8	85.1	7803	5	PCT-US93-12687-1	Sequence 1, Appli
	4	1743.4	81.2	7679	4	US-09-220-132-38	Sequence 38, Appl
	5	1743.4	81.2	7680	4	US-09-023-655-1289	Sequence 1289, Ap
	6	1743.4	81.2	7680	5	PCT-US95-09819-6	Sequence 6, Appli
	7	1740.2	81.1	7705	1	US-08-259-569-16	Sequence 16, Appl
	8	1740.2	81.1	7705	2	US-08-826-885-16	Sequence 16, Appl
	9	1738.6	81.0	7705	6	5455158-2	Patent No. 5455158
	10	1738.6	81.0	7705	6	5455158-2	Patent No. 5455158
	11	671.2	31.3	986	1	US-07-637-250A-8	Sequence 8, Appli
	12	671.2	31.3	986	1	US-08-145-061-8	Sequence 8, Appli
	13	97.4	4.5	186	1	US-08-153-799-5	Sequence 5, Appli
	14	73.8	3.4	2109	4	US-09-799-451-345	Sequence 345, App
	15	73.8	3.4	2334	4	US-09-023-655-996	Sequence 996, App
	16	73.8	3.4	2334	4	US-09-949-016-704	Sequence 704, App
	17	73.8	3.4	2335	4	US-09-799-451-346	Sequence 346, App
	18	73.8	3.4	2335	4	US-09-949-016-4758	Sequence 4758, Ap
	19	73.2	3.4	11665	4	US-09-949-016-12446	Sequence 12446, A
	20	73.2	3.4	11665	4	US-09-949-016-16500	Sequence 16500, A
c	21	72.4	3.4	85	1	US-08-259-569-28	Sequence 28, Appl
c	22	72.4	3.4	85	2	US-08-826-885-28	Sequence 28, Appl
	23	72.2	3.4	2334	1	US-08-457-304A-33	Sequence 33, Appl
	24	72.2	3.4	2334	1	US-08-456-701A-33	Sequence 33, Appl
	25	72.2	3.4	2334	3	US-08-684-932A-33	Sequence 33, Appl
	26	72	3.4	72	1	US-08-259-569-29	Sequence 29, Appl
	27	72	3.4	72	2	US-08-826-885-29	Sequence 29, Appl
	28	72	3.4	72	6	5455158-9	Patent No. 5455158
	29	72	3.4	72	6	5455158-9	Patent No. 5455158
	30	71.8	3.3	1983	4	US-09-949-016-2066	Sequence 2066, Ap
	31	71.8	3.3	3069	4	US-09-949-016-641	Sequence 641, App
	32	69	3.2	69	1	US-08-259-569-23	Sequence 23, Appl
	33	69	3.2	69	2	US-08-826-885-23	Sequence 23, Appl
	34	65.8	3.1	69	6	5455158-6	Patent No. 5455158
	35	65.8	3.1	69	6	5455158-6	Patent No. 5455158
c	36	65.4	3.0	69	1	US-08-259-569-30	Sequence 30, Appl
c	37	65.4	3.0	69	2	US-08-826-885-30	Sequence 30, Appl
	38	65.2	3.0	601	4	US-09-949-016-30391	Sequence 30391, A
	39	65.2	3.0	601	4	US-09-949-016-70165	Sequence 70165, A
	40	65.2	3.0	29954	4	US-09-949-016-13808	Sequence 13808, A
	41	65.2	3.0	31040	4	US-09-949-016-12383	Sequence 12383, A
c	42	65	3.0	75	1	US-08-259-569-18	Sequence 18, Appl
c	43	65	3.0	75	2	US-08-826-885-18	Sequence 18, Appl
	44	64.8	3.0	68	6	5455158-4	Patent No. 5455158
	45	64.8	3.0	68	6	5455158-4	Patent No. 5455158

ALIGNMENTS

RESULT 1
US-09-566-921-135
; Sequence 135, Application US/09566921
; Patent No. 6682888
; GENERAL INFORMATION:
; APPLICANT: Loring, Jeanne F.
; APPLICANT: Tingley, Debora W.
; APPLICANT: Edwards, Carla M.
; TITLE OF INVENTION: GENES EXPRESSED IN ALZHEIMER'S DISEASE
; FILE REFERENCE: PA-0024 US
; CURRENT APPLICATION NUMBER: US/09/566,921
; CURRENT FILING DATE: 2000-05-05
; NUMBER OF SEQ ID NOS: 138
; SOFTWARE: PERL Program
; SEQ ID NO 135
; LENGTH: 8044
; TYPE: DNA
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: misc_feature
; OTHER INFORMATION: Incyte ID No. 6682888 427813.14
US-09-566-921-135

Query Match 87.9%; Score 1887.4; DB 4; Length 8044;
Best Local Similarity 97.4%; Pred. No. 0;
Matches 1946; Conservative 0; Mismatches 6; Indels 45; Gaps 1;

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Qy          1 CAAACTTGGTGGCAACTTGCCTCCCGGTGCGGGCGTCTCTCCCCCACCGTCTCAACATGC 60
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Db        213 CAAACTTGGTGGCAACTTGCCTCCCGGTGCGGGCGTCTCTCCCCCACCGTCTCAACATGC 272

Qy         61 TTAGGGGTCCGGGGCCCCGGGCTGCTGCTGCTGGCCGTCCAGTGCCTGGGGACAGCGGTGC 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        273 TTAGGGGTCCGGGGCCCCGGGCTGCTGCTGCTGGCCGTCCTGTGCCTGGGGACAGCGGTGC 332

Qy        121 CCTCCACGGGAGCCTCGAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGCCCCAGTCCC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        333 CCTCCACGGGAGCCTCGAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGCCCCAGTCCC 392

Qy        181 CGGTGGCTGTCAGTCAAAGCAAGCCCGGTTGTTATGACAATGGAAAACACTATCAGATAA 240
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Db        393 CGGTGGCTGTCAGTCAAAGCAAGCCCGGTTGTTATGACAATGGAAAACACTATCAGATAA 452

Qy        241 ATCAACAGTGGGAGCGGACCTACCTAGGCAATGCGTTGGTTTGTACTTGTTATGGAGGAA 300
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Db        453 ATCAACAGTGGGAGCGGACCTACCTAGGCAATGCGTTGGTTTGTACTTGTTATGGAGGAA 512

Qy        301 GCCGAGGTTTTAACTGCGAGAGTAAACCTGAAGCTGAAGAGACTTGCTTTGACAAGTACA 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        513 GCCGAGGTTTTAACTGCGAGAGTAAACCTGAAGCTGAAGAGACTTGCTTTGACAAGTACA 572
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Qy       361 CTGGGAACACTTACCGAGTGGGTGACACTTATGAGCGTCCTAAAGACTCCATGATCTGGG 420
Db       573 CTGGGAACACTTACCGAGTGGGTGACACTTATGAGCGTCCTAAAGACTCCATGATCTGGG 632

Qy       421 ACTGTACCTGCATCGGGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTGCC 480
Db       633 ACTGTACCTGCATTGGGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTGCC 692

Qy       481 ATGAAGGGGGTCAGTCCTACAAGATTGGTGACACCTGGAGGAGACCACATGAGACTGGTG 540
Db       693 ATGAAGGGGGTCAGTCCTACAAGATTGGTGACACCTGGAGGAGACCACATGAGACTGGTG 752

Qy       541 GTTACATGTTAGAGTGTGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCTGCAAGCCCA 600
Db       753 GTTACATGTTAGAGTGTGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCTGCAAGCCCA 812

Qy       601 TAGCTGAGAAGTGTTTTGATCATGCTGCTGGGACTTCCTATGTGGTCGGAGAAACGTGGG 660
Db       813 TAGCTGAGAAGTGTTTTGATCATGCTGCTGGGACTTCCTATGTGGTCGGAGAAACGTGGG 872

Qy       661 AGAAGCCCTACCAAGGCTGGATGATGGTAGATTGTACTTGCCTGGGAGAAGGCAGCGGAC 720
Db       873 AGAAGCCCTACCAAGGCTGGATGATGGTAGATTGTACTTGCCTGGGAGAAGGCAGCGGAC 932

Qy       721 GCATCACTTGCACTTCTAGAAATAGATGCAACGATCAGGACACAAGGACATCCTATAGAA 780
Db       933 GCATCACTTGCACTTCTAGAAATAGATGCAACGATCAGGACACAAGGACATCCTATAGAA 992

Qy       781 TTGGAGACACCTGGAGCAAGAAGGATAATCGAGGAAACCTGCTCCAGTGCATCTGCACAG 840
Db       993 TTGGAGACACCTGGAGCAAGAAGGATAATCGAGGAAACCTGCTCCAGTGCATCTGCACAG 1052

Qy       841 GCAACGGCCGAGGAGAGTGGAAGTGTGAGAGGCACACCTCTGTGCAGACCACATCGAGCG 900
Db      1053 GCAACGGCCGAGGAGAGTGGAAGTGTGAGAGGCACACCTCTGTGCAGACCACATCGAGCG 1112

Qy       901 GATCTGGCCCCTTCACCGATGTTCGTGCAGCTGTTTACCAACCGCAGCCTCACCCCCAGC 960
Db      1113 GATCTGGCCCCTTCACCGATGTTCGTGCAGCTGTTTACCAACCGCAGCCTCACCCCCAGC 1172

Qy       961 CTCCTCCCTATGGCCACTGTGTCACAGACAGTGGTGTGGTCTACTCTGTGGGGATGCAGT 1020
Db      1173 CTCCTCCCTATGGCCACTGTGTCACAGACAGTGGTGTGGTCTACTCTGTGGGGATGCAGT 1232

Qy      1021 GGCTGAAGACACAAGGAAATAAGCAAATGCTTTGCACGTGCCTGGGCAACGGAGTCAGCT 1080
Db      1233 GGCTGAAGACACAAGGAAATAAGCAAATGCTTTGCACGTGCCTGGGCAACGGAGTCAGCT 1292

Qy      1081 GCCAAGAGACAGCTGTAACCCAGACTTACGGTGGCAACTCAAATGGAGAGCCATGTGTCT 1140
Db      1293 GCCAAGAGACAGCTGTAACCCAGACTTACGGTGGCAACTCAAATGGAGAGCCATGTGTCT 1352

Qy      1141 TACCATTCACCTACAACGACAGGAC---------------------------------- 1165
Db      1353 TACCATTCACCTACAATGGCAGGACGTTCTACTCCTGCACCACAGAAGGGCGACAGGACG 1412

Qy      1166 ----------GGACAGCACAACTTCGAATTATGAGCAGGACCAGAAATACTCTTTCTGCA 1215
Db      1413 GACATCTTTGGTGCAGCACAACTTCGAATTATGAGCAGGACCAGAAATACTCTTTCTGCA 1472

Qy      1216 CAGACCACACTGTTTTGGTTCAGACTCGAGGAGGAAATTCCAATGGTGCCTTGTGCCACT 1275
Db      1473 CAGACCACACTGTTTTGGTTCAGACTCGAGGAGGAAATTCCAATGGTGCCTTGTGCCACT 1532

Qy      1276 TCCCCTTCCTATACAACAACCACAATTACACTGATTGCACTTCTGAGGGCAGAAGAGACA 1335
Db      1533 TCCCCTTCCTATACAACAACCACAATTACACTGATTGCACTTCTGAGGGCAGAAGAGACA 1592

Qy      1336 ACATGAAGTGGTGTGGGACCACACAGAACTATGATGCCGACCAGAAGTTTGGGTTCTGCC 1395
Db      1593 ACATGAAGTGGTGTGGGACCACACAGAACTATGATGCCGACCAGAAGTTTGGGTTCTGCC 1652

Qy      1396 CCATGGCTGCCCACGAGGAAATCTGCACAACCAATGAAGGGGTCATGTACCGCATTGGAG 1455
Db      1653 CCATGGCTGCCCACGAGGAAATCTGCACAACCAATGAAGGGGTCATGTACCGCATTGGAG 1712

Qy      1456 ATCAGTGGGATAAGCAGCATGACATGGGTCACATGATGAGGTGCACGTGTGTTGGGAATG 1515
Db      1713 ATCAGTGGGATAAGCAGCATGACATGGGTCACATGATGAGGTGCACGTGTGTTGGGAATG 1772

Qy      1516 GTCGTGGGGAATGGACATGCATTGCCTACTCGCAGCTTCGAGATCAGTGCATTGTTGATG 1575
Db      1773 GTCGTGGGGAATGGACATGCATTGCCTACTCGCAGCTTCGAGATCAGTGCATTGTTGATG 1832

Qy      1576 ACATCACTTACAATGTGAACGACACATTCCACAAGCGTCATGAAGAGGGGCACATGCTGA 1635
Db      1833 ACATCACTTACAATGTGAACGACACATTCCACAAGCGTCATGAAGAGGGGCACATGCTGA 1892

Qy      1636 ACTGTACATGCTTCGGTCAGGGTCGGGGCAGGTGGAAGTGTGATCCCGTCGACCAATGCC 1695
Db      1893 ACTGTACATGCTTCGGTCAGGGTCGGGGCAGGTGGAAGTGTGATCCCGTCGACCAATGCC 1952

Qy      1696 AGGATTCAGAGACTGGGACGTTTTATCAAATTGGAGATTCATGGGAGAAGTATGTGCATG 1755
Db      1953 AGGATTCAGAGACTGGGACGTTTTATCAAATTGGAGATTCATGGGAGAAGTATGTGCATG 2012

Qy      1756 GTGTCAGATACCAGTGCTACTGCTATGGCCGTGGCATTGGGGAGTGGCATTGCCAACCTT 1815
Db      2013 GTGTCAGATACCAGTGCTACTGCTATGGCCGTGGCATTGGGGAGTGGCATTGCCAACCTT 2072

Qy      1816 TACAGACCTATCCAAGCTCAAGTGGTCCTGTCGAAGTATTTATCACTGAGACTCCGAGTC 1875
Db      2073 TACAGACCTATCCAAGCTCAAGTGGTCCTGTCGAAGTATTTATCACTGAGACTCCGAGTC 2132

Qy      1876 AGCCCAACTCCCACCCCATCCAGTGGAATGCACCACAGCCATCTCACATTTCCAAGTACA 1935
Db      2133 AGCCCAACTCCCACCCCATCCAGTGGAATGCACCACAGCCATCTCACATTTCCAAGTACA 2192

Qy      1936 TTCTCAGGTGGAGACCT 1952
Db      2193 TTCTCAGGTGGAGACCT 2209
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RESULT 2
US-08-551-356-1
; Sequence 1, Application US/08551356
; Patent No. 5830700
; GENERAL INFORMATION:
; APPLICANT: Irani, Meher
; TITLE OF INVENTION: HYBRID CROSS-LINKING PROTEINS
; NUMBER OF SEQUENCES: 14
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: ZymoGenetics, Inc.
; STREET: 4225 Roosevelt Way, N.E.
; CITY: Seattle
; STATE: WA
; COUNTRY: USA
; ZIP: 98105
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/551,356
; FILING DATE:
; CLASSIFICATION: 435
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US/08/349,762
; FILING DATE:
; APPLICATION NUMBER: US/07/998,271
; FILING DATE:
; ATTORNEY/AGENT INFORMATION:
; NAME: Holly, Julie A
; REGISTRATION NUMBER: 33-246

```
;      REFERENCE/DOCKET NUMBER:  92-26
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  206-547-8080 ext 322
;      TELEFAX:  206-548-2329
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  7803 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    FEATURE:
;      NAME/KEY:  CDS
;      LOCATION:  6..7346
US-08-551-356-1

  Query Match             85.1%;  Score 1826.8;  DB 2;  Length 7803;
  Best Local Similarity   97.1%;  Pred. No. 0;
  Matches 1889;  Conservative    0;  Mismatches   12;  Indels   45;  Gaps    1;

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Db          1 TCAACATGCTTAGGGGTCCGGGGCCCGGGCTGCTGCTGCTGGCCGTCCTGTGCCTGGGGA 60

Qy        112 CAGCGGTGCCCTCCACGGGAGCCTCGAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGC 171
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 CAGCGGTGCCCTCCACGGGAGCCTCGAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGC 120

Qy        172 CCCAGTCCCCGGTGGCTGTCAGTCAAAGCAAGCCCGGTTGTTATGACAATGGAAAACACT 231
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Db        121 CCCAGTCCCCGGTGGCTGTCAGTCAAAGCAAGCCCGGTTGTTATGACAATGGAAAACACT 180

Qy        232 ATCAGATAAATCAACAGTGGGAGCGGACCTACCTAGGCAATGCGTTGGTTTGTACTTGTT 291
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Db        181 ATCAGATAAATCAACAGTGGGAGCGGACCTACCTAGGTAATGTGTTGGTTTGTACTTGTT 240

Qy        292 ATGGAGGAAGCCGAGGTTTTAACTGCGAGAGTAAACCTGAAGCTGAAGAGACTTGCTTTG 351
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Db        241 ATGGAGGAAGCCGAGGTTTTAACTGCGAAAGTAAACCTGAAGCTGAAGAGACTTGCTTTG 300

Qy        352 ACAAGTACACTGGGAACACTTACCGAGTGGGTGACACTTATGAGCGTCCTAAAGACTCCA 411
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Db        301 ACAAGTACACTGGGAACACTTACCGAGTGGGTGACACTTATGAGCGTCCTAAAGACTCCA 360

Qy        412 TGATCTGGGACTGTACCTGCATCGGGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAA 471
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Db        361 TGATCTGGGACTGTACCTGCATCGGGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAA 420

Qy        472 ACCGCTGCCATGAAGGGGGTCAGTCCTACAAGATTGGTGACACCTGGAGGAGACCACATG 531
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Db        421 ACCGCTGCCATGAAGGGGGTCAGTCCTACAAGATTGGTGACACCTGGAGGAGACCACATG 480

Qy        532 AGACTGGTGGTTACATGTTAGAGTGTGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCT 591
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Db        481 AGACTGGTGGTTACATGTTAGAGTGTGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCT 540

Qy        592 GCAAGCCCATAGCTGAGAAGTGTTTTGATCATGCTGCTGGGACTTCCTATGTGGTCGGAG 651
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 GCAAGCCCATAGCTGAGAAGTGTTTTGATCATGCTGCTGGGACTTCCTATGTGGTCGGAG 600

Qy        652 AAACGTGGGAGAAGCCCTACCAAGGCTGGATGATGGTAGATTGTACTTGCCTGGGAGAAG 711
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Db        601 AAACGTGGGAGAAGCCCTACCAAGGCTGGATGATGGTAGATTGTACTTGCCTGGGAGAAG 660

Qy        712 GCAGCGGACGCATCACTTGCACTTCTAGAAATAGATGCAACGATCAGGACACAAGGACAT 771
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Db        661 GCAGCGGACGCATCACTTGCACTTCTAGAAATAGATGCAACGATCAGGACACAAGGACAT 720

Qy        772 CCTATAGAATTGGAGACACCTGGAGCAAGAAGGATAATCGAGGAAACCTGCTCCAGTGCA 831
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Db        721 CCTATAGAATTGGAGACACCTGGAGCAAGAAGGATAATCGAGGAAACCTGCTCCAGTGCA 780

Qy        832 TCTGCACAGGCAACGGCCGAGGAGAGTGGAAGTGTGAGAGGCACACCTCTGTGCAGACCA 891
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        781 TCTGCACAGGCAACGGCCGAGGAGAGTGGAAGTGTGAGAGGCACACCTCTGTGCAGACCA 840

Qy        892 CATCGAGCGGATCTGGCCCCTTCACCGATGTTCGTGCAGCTGTTTACCAACCGCAGCCTC 951
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Db        841 CATCGAGCGGATCTGGCCCCTTCACCGATGTTCGTGCAGCTGTTTACCAACCGCAGCCTC 900

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Db        901 ACCCCCAGCCTCCTCCCTATGGCCACTGTGTCACAGACAGTGGTGTGGTCTACTCTGTGG 960

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              |||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Db       1021 GAGTCAGCTGCCAAGAGACAGCTGTAACCCAGACTTACGGTGGCAACTTAAATGGAGAGC 1080

Qy       1132 CATGTGTCTTACCATTCACCTACAACGACAGGAC-------------------------- 1165
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Db       1081 CATGTGTCTTACCATTCACCTACAATGGCAGGACGTTCTACTCCTGCACCACGGAAGGGC 1140

Qy       1166 ------------------GGACAGCACAACTTCGAATTATGAGCAGGACCAGAAATACT 1206
                               | ||||||||||||||||||||||||||||||||||||||
Db       1141 GACAGGACGGACATCTTTGGTGCAGCACAACTTCGAATTATGAGCAGGACCAGAAATACT 1200

Qy       1207 CTTTCTGCACAGACCACACTGTTTTGGTTCAGACTCGAGGAGGAAATTCCAATGGTGCCT 1266
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Db       1201 CTTTCTGCACAGACCACACTGTTTTGGTTCAGACTCAAGGAGGAAATTCCAATGGTGCCT 1260

Qy       1267 TGTGCCACTTCCCCTTCCTATACAACAACCACAATTACACTGATTGCACTTCTGAGGGCA 1326
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Db       1261 TGTGCCACTTCCCCTTCCTATACAACAACCACAATTACACTGATTGCACTTCTGAGGGCA 1320

Qy       1327 GAAGAGACAACATGAAGTGGTGTGGGACCACACAGAACTATGATGCCGACCAGAAGTTTG 1386
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Db       1321 GAAGAGACAACATGAAGTGGTGTGGGACCACACAGAACTATGATGCCGACCAGAAGTTTG 1380

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Db       1381 GGTTCTGCCCCATGGCTGCCCACGAGGAAATCTGCACAACCAATGAAGGGGTCATGTACC 1440

Qy       1447 GCATTGGAGATCAGTGGGATAAGCAGCATGACATGGGTCACATGATGAGGTGCACGTGTG 1506
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Db       1441 GCATTGGAGATCAGTGGGATAAGCAGCATGACATGGGTCACATGATGAGGTGCACGTGTG 1500

Qy       1507 TTGGGAATGGTCGTGGGGAATGGACATGCATTGCCTACTCGCAGCTTCGAGATCAGTGCA 1566
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Db       1501 TTGGGAATGGTCGTGGGGAATGGACATGCATTGCCTACTCGCAACTTCGAGATCAGTGCA 1560

Qy       1567 TTGTTGATGACATCACTTACAATGTGAACGACACATTCCACAAGCGTCATGAAGAGGGGC 1626
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Db       1561 TTGTTGATGACATCACTTACAATGTGAACGACACATTCCACAAGCGTCATGAAGAGGGGC 1620

Qy       1627 ACATGCTGAACTGTACATGCTTCGGTCAGGGTCGGGGCAGGTGGAAGTGTGATCCCGTCG 1686
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Db       1621 ACATGCTGAACTGTACATGCTTCGGTCAGGGTCGGGGCAGGTGGAAGTGTGATCCCGTCG 1680

Qy       1687 ACCAATGCCAGGATTCAGAGACTGGGACGTTTTATCAAATTGGAGATTCATGGGAGAAGT 1746
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 ACCAATGCCAGGATTCAGAGACTGGGACGTTTTATCAAATTGGAGATTCATGGGAGAAGT 1740

Qy       1747 ATGTGCATGGTGTCAGATACCAGTGCTACTGCTATGGCCGTGGCATTGGGGAGTGGCATT 1806
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 ATGTGCATGGTGTCAGATACCAGTGCTACTGCTATGGCCGTGGCATTGGGGAGTGGCATT 1800

Qy       1807 GCCAACCTTTACAGACCTATCCAAGCTCAAGTGGTCCTGTCGAAGTATTTATCACTGAGA 1866
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Db       1801 GCCAACCTTTACAGACCTATCCAAGCTCAAGTGGTCCTGTCGAAGTATTTATCACTGAGA 1860

Qy       1867 CTCCGAGTCAGCCCAACTCCCACCCCATCCAGTGGAATGCACCACAGCCATCTCACATTT 1926
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Db       1861 CTCCGAGTCAGCCCAACTCCCACCCCATCCAGTGGAATGCACCACAGCCATCTCACATTT 1920
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Qy       1927 CCAAGTACATTCTCAGGTGGAGACCT 1952
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Db       1921 CCAAGTACATTCTCAGGTGGAGACCT 1946
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RESULT 3
PCT-US93-12687-1
; Sequence 1, Application PC/TUS9312687
; GENERAL INFORMATION:
; APPLICANT: Irani, Meher H.
; TITLE OF INVENTION: HYBRID CROSS-LINKING PROTEINS
; NUMBER OF SEQUENCES: 14
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: ZymoGenetics, Inc.
; STREET: 4225 Roosevelt Way, N.E.
; CITY: Seattle
; STATE: WA
; COUNTRY: USA
; ZIP: 98105
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: PCT/US93/12687
; FILING DATE:
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 07/998,271
; FILING DATE: 31-DEC-1992
; ATTORNEY/AGENT INFORMATION:
; NAME: Parker, Gary E
; REGISTRATION NUMBER: 31-648
; REFERENCE/DOCKET NUMBER: 92-26PC
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 206-547-8080 ext 322
; TELEFAX: 206-548-2329
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 7803 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 6..7346
PCT-US93-12687-1

Query Match 85.1%; Score 1826.8; DB 5; Length 7803;
Best Local Similarity 97.1%; Pred. No. 0;
Matches 1889; Conservative 0; Mismatches 12; Indels 45; Gaps 1;

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Qy         52 TCAACATGCTTAGGGGTCCGGGGCCCGGGCTGCTGCTGCTGGCCGTCCAGTGCCTGGGGA 111
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 TCAACATGCTTAGGGGTCCGGGGCCCGGGCTGCTGCTGCTGGCCGTCCTGTGCCTGGGGA 60

Qy        112 CAGCGGTGCCCTCCACGGGAGCCTCGAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGC 171
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 CAGCGGTGCCCTCCACGGGAGCCTCGAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGC 120

Qy        172 CCCAGTCCCCGGTGGCTGTCAGTCAAAGCAAGCCCGGTTGTTATGACAATGGAAAACACT 231
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 CCCAGTCCCCGGTGGCTGTCAGTCAAAGCAAGCCCGGTTGTTATGACAATGGAAAACACT 180

Qy        232 ATCAGATAAATCAACAGTGGGAGCGGACCTACCTAGGCAATGCGTTGGTTTGTACTTGTT 291
              ||||||||||||||||||||||||||||||||||| |||| ||||||||||||||||||
Db        181 ATCAGATAAATCAACAGTGGGAGCGGACCTACCTAGGTAATGTGTTGGTTTGTACTTGTT 240

Qy        292 ATGGAGGAAGCCGAGGTTTTAACTGCGAGAGTAAACCTGAAGCTGAAGAGACTTGCTTTG 351
              |||||||||||||||||||||||||| |||||||||||||||||||||||||||||||
Db        241 ATGGAGGAAGCCGAGGTTTTAACTGCGAAAGTAAACCTGAAGCTGAAGAGACTTGCTTTG 300

Qy        352 ACAAGTACACTGGGAACACTTACCGAGTGGGTGACACTTATGAGCGTCCTAAAGACTCCA 411
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 ACAAGTACACTGGGAACACTTACCGAGTGGGTGACACTTATGAGCGTCCTAAAGACTCCA 360

Qy        412 TGATCTGGGACTGTACCTGCATCGGGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAA 471
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Db        361 TGATCTGGGACTGTACCTGCATCGGGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAA 420

Qy        472 ACCGCTGCCATGAAGGGGGTCAGTCCTACAAGATTGGTGACACCTGGAGGAGACCACATG 531
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 ACCGCTGCCATGAAGGGGGTCAGTCCTACAAGATTGGTGACACCTGGAGGAGACCACATG 480

Qy        532 AGACTGGTGGTTACATGTTAGAGTGTGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCT 591
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Db        481 AGACTGGTGGTTACATGTTAGAGTGTGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCT 540

Qy        592 GCAAGCCCATAGCTGAGAAGTGTTTTGATCATGCTGCTGGGACTTCCTATGTGGTCGGAG 651
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Db        541 GCAAGCCCATAGCTGAGAAGTGTTTTGATCATGCTGCTGGGACTTCCTATGTGGTCGGAG 600

Qy        652 AAACGTGGGAGAAGCCCTACCAAGGCTGGATGATGGTAGATTGTACTTGCCTGGGAGAAG 711
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Db        601 AAACGTGGGAGAAGCCCTACCAAGGCTGGATGATGGTAGATTGTACTTGCCTGGGAGAAG 660

Qy        712 GCAGCGGACGCATCACTTGCACTTCTAGAAATAGATGCAACGATCAGGACACAAGGACAT 771
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 GCAGCGGACGCATCACTTGCACTTCTAGAAATAGATGCAACGATCAGGACACAAGGACAT 720

Qy        772 CCTATAGAATTGGAGACACCTGGAGCAAGAAGGATAATCGAGGAAACCTGCTCCAGTGCA 831
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 CCTATAGAATTGGAGACACCTGGAGCAAGAAGGATAATCGAGGAAACCTGCTCCAGTGCA 780

Qy        832 TCTGCACAGGCAACGGCCGAGGAGAGTGGAAGTGTGAGAGGCACACCTCTGTGCAGACCA 891
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 TCTGCACAGGCAACGGCCGAGGAGAGTGGAAGTGTGAGAGGCACACCTCTGTGCAGACCA 840

Qy        892 CATCGAGCGGATCTGGCCCCTTCACCGATGTTCGTGCAGCTGTTTACCAACCGCAGCCTC 951
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 CATCGAGCGGATCTGGCCCCTTCACCGATGTTCGTGCAGCTGTTTACCAACCGCAGCCTC 900

Qy        952 ACCCCCAGCCTCCTCCCTATGGCCACTGTGTCACAGACAGTGGTGTGGTCTACTCTGTGG 1011
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 ACCCCCAGCCTCCTCCCTATGGCCACTGTGTCACAGACAGTGGTGTGGTCTACTCTGTGG 960

Qy       1012 GGATGCAGTGGCTGAAGACACAAGGAAATAAGCAAATGCTTTGCACGTGCCTGGGCAACG 1071
              |||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 GGATGCAGTGGTTGAAGACACAAGGAAATAAGCAAATGCTTTGCACGTGCCTGGGCAACG 1020

Qy       1072 GAGTCAGCTGCCAAGAGACAGCTGTAACCCAGACTTACGGTGGCAACTCAAATGGAGAGC 1131
              |||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Db       1021 GAGTCAGCTGCCAAGAGACAGCTGTAACCCAGACTTACGGTGGCAACTTAAATGGAGAGC 1080

Qy       1132 CATGTGTCTTACCATTCACCTACAACGACAGGAC------------------------- 1165
              |||||||||||||||||||||||| | ||||||
Db       1081 CATGTGTCTTACCATTCACCTACAATGGCAGGACGTTCTACTCCTGCACCACGGAAGGGC 1140

Qy       1166 ------------------GGACAGCACAACTTCGAATTATGAGCAGGACCAGAAATACT 1206
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Db       1141 GACAGGACGGACATCTTTGGTGCAGCACAACTTCGAATTATGAGCAGGACCAGAAATACT 1200

Qy       1207 CTTTCTGCACAGACCACACTGTTTTGGTTCAGACTCGAGGAGGAAATTCCAATGGTGCCT 1266
              |||||||||||||||||||||||||||||||||| ||||||||||||||||||||||||
Db       1201 CTTTCTGCACAGACCACACTGTTTTGGTTCAGACTCAAGGAGGAAATTCCAATGGTGCCT 1260

Qy       1267 TGTGCCACTTCCCCTTCCTATACAACAACCACAATTACACTGATTGCACTTCTGAGGGCA 1326
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 TGTGCCACTTCCCCTTCCTATACAACAACCACAATTACACTGATTGCACTTCTGAGGGCA 1320

Qy       1327 GAAGAGACAACATGAAGTGGTGTGGGACCACACAGAACTATGATGCCGACCAGAAGTTTG 1386
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 GAAGAGACAACATGAAGTGGTGTGGGACCACACAGAACTATGATGCCGACCAGAAGTTTG 1380
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Qy       1387 GGTTCTGCCCCATGGCTGCCCACGAGGAAATCTGCACAACCAATGAAGGGGTCATGTACC 1446
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 GGTTCTGCCCCATGGCTGCCCACGAGGAAATCTGCACAACCAATGAAGGGGTCATGTACC 1440

Qy       1447 GCATTGGAGATCAGTGGGATAAGCAGCATGACATGGGTCACATGATGAGGTGCACGTGTG 1506
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 GCATTGGAGATCAGTGGGATAAGCAGCATGACATGGGTCACATGATGAGGTGCACGTGTG 1500

Qy       1507 TTGGGAATGGTCGTGGGGAATGGACATGCATTGCCTACTCGCAGCTTCGAGATCAGTGCA 1566
             |||||||||||||||||||||||||||||||||||||||||| ||||||||||||||||||
Db       1501 TTGGGAATGGTCGTGGGGAATGGACATGCATTGCCTACTCGCAACTTCGAGATCAGTGCA 1560

Qy       1567 TTGTTGATGACATCACTTACAATGTGAACGACACATTCCACAAGCGTCATGAAGAGGGGC 1626
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 TTGTTGATGACATCACTTACAATGTGAACGACACATTCCACAAGCGTCATGAAGAGGGGC 1620

Qy       1627 ACATGCTGAACTGTACATGCTTCGGTCAGGGTCGGGGCAGGTGGAAGTGTGATCCCGTCG 1686
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 ACATGCTGAACTGTACATGCTTCGGTCAGGGTCGGGGCAGGTGGAAGTGTGATCCCGTCG 1680

Qy       1687 ACCAATGCCAGGATTCAGAGACTGGGACGTTTTATCAAATTGGAGATTCATGGGAGAAGT 1746
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 ACCAATGCCAGGATTCAGAGACTGGGACGTTTTATCAAATTGGAGATTCATGGGAGAAGT 1740

Qy       1747 ATGTGCATGGTGTCAGATACCAGTGCTACTGCTATGGCCGTGGCATTGGGGAGTGGCATT 1806
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 ATGTGCATGGTGTCAGATACCAGTGCTACTGCTATGGCCGTGGCATTGGGGAGTGGCATT 1800

Qy       1807 GCCAACCTTTACAGACCTATCCAAGCTCAAGTGGTCCTGTCGAAGTATTTATCACTGAGA 1866
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 GCCAACCTTTACAGACCTATCCAAGCTCAAGTGGTCCTGTCGAAGTATTTATCACTGAGA 1860

Qy       1867 CTCCGAGTCAGCCCAACTCCCACCCCATCCAGTGGAATGCACCACAGCCATCTCACATTT 1926
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 CTCCGAGTCAGCCCAACTCCCACCCCATCCAGTGGAATGCACCACAGCCATCTCACATTT 1920

Qy       1927 CCAAGTACATTCTCAGGTGGAGACCT 1952
             |||||||||||||||||||||||||
Db       1921 CCAAGTACATTCTCAGGTGGAGACCT 1946
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RESULT 4
US-09-220-132-38
; Sequence 38, Application US/09220132
; Patent No. 6506607
; GENERAL INFORMATION:
; APPLICANT: Shyjan, Andrew W.
; TITLE OF INVENTION: METHODS AND COMPOSITONS FOR THE IDENTIFICATION AND ASSESSMENT
; TITLE OF INVENTION: OF PROSTATE CANCER THERAPIES AND THE DIAGNOSIS OF PROSTATE CANCE
; FILE REFERENCE: 07334-074001
; CURRENT APPLICATION NUMBER: US/09/220,132
; CURRENT FILING DATE: 1998-12-23
; PRIOR APPLICATION NUMBER: US 60/079,303
; PRIOR FILING DATE: 1998-03-25
; PRIOR APPLICATION NUMBER: US 60/068,821
; PRIOR FILING DATE: 1997-12-24
; NUMBER OF SEQ ID NOS: 191
; SOFTWARE: PastSEQ for Windows Version 4.0
; SEQ ID NO 38
; LENGTH: 7679
; TYPE: DNA
; ORGANISM: Homo sapiens
US-09-220-132-38

Query Match 81.2%; Score 1743.4; DB 4; Length 7679;
Best Local Similarity 97.0%; Pred. No. 0;
Matches 1805; Conservative 0; Mismatches 11; Indels 45; Gaps 1;

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Qy        137 GAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGCCCCAGTCCCCGGTGGCTGTCAGTCA 196
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 GAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGCCCCAGTCCCCGGTGGCTGTCAGTCA 60

Qy        197 AAGCAAGCCCGGTTGTTATGACAATGGAAAACACTATCAGATAAATCAACAGTGGGAGCG 256
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 AAGCAAGCCCGGTTGTTATGACAATGGAAAACACTATCAGATAAATCAACAGTGGGAGCG 120

Qy        257 GACCTACCTAGGCAATGCGTTGGTTTGTACTTGTTATGGAGGAAGCCGAGGTTTTAACTG 316
              |||||||||||| |||| ||||||||||||||||||||||||||||||||||||||||||||
Db        121 GACCTACCTAGGTAATGTGTTGGTTTGTACTTGTTATGGAGGAAGCCGAGGTTTTAACTG 180

Qy        317 CGAGAGTAAACCTGAAGCTGAAGAGACTTGCTTTGACAAGTACACTGGGAACACTTACCG 376
              ||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 CGAAAGTAAACCTGAAGCTGAAGAGACTTGCTTTGACAAGTACACTGGGAACACTTACCG 240

Qy        377 AGTGGGTGACACTTATGAGCGTCCTAAAGACTCCATGATCTGGGACTGTACCTGCATCGG 436
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AGTGGGTGACACTTATGAGCGTCCTAAAGACTCCATGATCTGGGACTGTACCTGCATCGG 300

Qy        437 GGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTGCCATGAAGGGGGTCAGTC 496
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTGCCATGAAGGGGGTCAGTC 360

Qy        497 CTACAAGATTGGTGACACCTGGAGGAGACCACATGAGACTGGTGGTTACATGTTAGAGTG 556
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 CTACAAGATTGGTGACACCTGGAGGAGACCACATGAGACTGGTGGTTACATGTTAGAGTG 420

Qy        557 TGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCTGCAAGCCCATAGCTGAGAAGTGTTT 616
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 TGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCTGCAAGCCCATAGCTGAGAAGTGTTT 480

Qy        617 TGATCATGCTGCTGGGACTTCCTATGTGGTCGGAGAAACGTGGGAGAAGCCCTACCAAGG 676
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Db        481 TGATCATGCTGCTGGGACTTCCTATGTGGTCGGAGAAACGTGGGAGAAGCCCTACCAAGG 540

Qy        677 CTGGATGATGGTAGATTGTACTTGCCTGGGAGAAGGCAGCGGACGCATCACTTGCACTTC 736
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 CTGGATGATGGTAGATTGTACTTGCCTGGGAGAAGGCAGCGGACGCATCACTTGCACTTC 600

Qy        737 TAGAAATAGATGCAACGATCAGGACACAAGGACATCCTATAGAATTGGAGACACCTGGAG 796
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Db        601 TAGAAATAGATGCAACGATCAGGACACAAGGACATCCTATAGAATTGGAGACACCTGGAG 660

Qy        797 CAAGAAGGATAATCGAGGAAACCTGCTCCAGTGCATCTGCACAGGCAACGGCCGAGGAGA 856
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 CAAGAAGGATAATCGAGGAAACCTGCTCCAGTGCATCTGCACAGGCAACGGCCGAGGAGA 720

Qy        857 GTGGAAGTGTGAGAGGCACACCTCTGTGCAGACCACATCGAGCGGATCTGGCCCCTTCAC 916
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GTGGAAGTGTGAGAGGCACACCTCTGTGCAGACCACATCGAGCGGATCTGGCCCCTTCAC 780

Qy        917 CGATGTTCGTGCAGCTGTTTACCAACCGCAGCCTCACCCCCAGCCTCCTCCCTATGGCCA 976
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 CGATGTTCGTGCAGCTGTTTACCAACCGCAGCCTCACCCCCAGCCTCCTCCCTATGGCCA 840

Qy        977 CTGTGTCACAGACAGTGGTGTGGTCTACTCTGTGGGGATGCAGTGGCTGAAGACACAAGG 1036
              |||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||||
Db        841 CTGTGTCACAGACAGTGGTGTGGTCTACTCTGTGGGGATGCAGTGGTTGAAGACACAAGG 900

Qy       1037 AAATAAGCAAATGCTTTGCACGTGCCTGGGCAACGGAGTCAGCTGCCAAGAGACAGCTGT 1096
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 AAATAAGCAAATGCTTTGCACGTGCCTGGGCAACGGAGTCAGCTGCCAAGAGACAGCTGT 960

Qy       1097 AACCCAGACTTACGGTGGCAACTCAAATGGAGAGCCATGTGTCTTACCATTCACCTACAA 1156
              |||||||||||||||||||| ||||||||||||||||||||||||||||||||||||||||
Db        961 AACCCAGACTTACGGTGGCAACTTAAATGGAGAGCCATGTGTCTTACCATTCACCTACAA 1020

Qy       1157 CGACAGGAC----------------------------------------------GGACAG 1171
              | ||||||                                              | |||
Db       1021 TGGCAGGACGTTCTACTCCTGCACCACGGAAGGGCGACAGGACGGACATCTTTGGTGCAG 1080

Qy       1172 CACAACTTCGAATTATGAGCAGGACCAGAAATACTCTTTCTGCACAGACCACACTGTTTT 1231
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 CACAACTTCGAATTATGAGCAGGACCAGAAATACTCTTTCTGCACAGACCACACTGTTTT 1140

Qy       1232 GGTTCAGACTCGAGGAGGAAATTCCAATGGTGCCTTGTGCCACTTCCCCTTCCTATACAA 1291
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Db       1141 GGTTCAGACTCAAGGAGGAAATTCCAATGGTGCCTTGTGCCACTTCCCCTTCCTATACAA 1200

Qy       1292 CAACCACAATTACACTGATTGCACTTCTGAGGGCAGAAGAGACAACATGAAGTGGTGTGG 1351
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 CAACCACAATTACACTGATTGCACTTCTGAGGGCAGAAGAGACAACATGAAGTGGTGTGG 1260

Qy       1352 GACCACACAGAACTATGATGCCGACCAGAAGTTTGGGTTCTGCCCCATGGCTGCCCACGA 1411
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Db       1261 GACCACACAGAACTATGATGCCGACCAGAAGTTTGGGTTCTGCCCCATGGCTGCCCACGA 1320

Qy       1412 GGAAATCTGCACAACCAATGAAGGGGTCATGTACCGCATTGGAGATCAGTGGGATAAGCA 1471
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Db       1321 GGAAATCTGCACAACCAATGAAGGGGTCATGTACCGCATTGGAGATCAGTGGGATAAGCA 1380

Qy       1472 GCATGACATGGGTCACATGATGAGGTGCACGTGTGTTGGGAATGGTCGTGGGGAATGGAC 1531
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 GCATGACATGGGTCACATGATGAGGTGCACGTGTGTTGGGAATGGTCGTGGGGAATGGAC 1440

Qy       1532 ATGCATTGCCTACTCGCAGCTTCGAGATCAGTGCATTGTTGATGACATCACTTACAATGT 1591
             ||||||||||||||||| |||||||||||||||||||||||||||||||||||||||||||||
Db       1441 ATGCATTGCCTACTCGCAACTTCGAGATCAGTGCATTGTTGATGACATCACTTACAATGT 1500

Qy       1592 GAACGACACATTCCACAAGCGTCATGAAGAGGGGCACATGCTGAACTGTACATGCTTCGG 1651
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 GAACGACACATTCCACAAGCGTCATGAAGAGGGGCACATGCTGAACTGTACATGCTTCGG 1560

Qy       1652 TCAGGGTCGGGGCAGGTGGAAGTGTGATCCCGTCGACCAATGCCAGGATTCAGAGACTGG 1711
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Db       1561 TCAGGGTCGGGGCAGGTGGAAGTGTGATCCCGTCGACCAATGCCAGGATTCAGAGACTGG 1620

Qy       1712 GACGTTTTATCAAATTGGAGATTCATGGGAGAAGTATGTGCATGGTGTCAGATACCAGTG 1771
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Db       1621 GACGTTTTATCAAATTGGAGATTCATGGGAGAAGTATGTGCATGGTGTCAGATACCAGTG 1680

Qy       1772 CTACTGCTATGGCCGTGGCATTGGGGAGTGGCATTGCCAACCTTTACAGACCTATCCAAG 1831
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Db       1681 CTACTGCTATGGCCGTGGCATTGGGGAGTGGCATTGCCAACCTTTACAGACCTATCCAAG 1740

Qy       1832 CTCAAGTGGTCCTGTCGAAGTATTTATCACTGAGACTCCGAGTCAGCCCAACTCCCACCC 1891
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 CTCAAGTGGTCCTGTCGAAGTATTTATCACTGAGACTCCGAGTCAGCCCAACTCCCACCC 1800

Qy       1892 CATCCAGTGGAATGCACCACAGCCATCTCACATTTCCAAGTACATTCTCAGGTGGAGACC 1951
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 CATCCAGTGGAATGCACCACAGCCATCTCACATTTCCAAGTACATTCTCAGGTGGAGACC 1860

Qy       1952 T 1952
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Db       1861 T 1861
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RESULT 5
US-09-023-655-1289
; Sequence 1289, Application US/09023655
; Patent No. 6607879
;  GENERAL INFORMATION:
;    APPLICANT:  Cocks, Benjamin G.
;    APPLICANT:  Susan G. Stuart
;    APPLICANT:  Jeffrey J. Seilhamer
;    TITLE OF INVENTION:  COMPOSITION FOR THE DETECTION OF BLOOD CELL GENE
;    TITLE OF INVENTION:  EXPRESSION
;    NUMBER OF SEQUENCES:  1508
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  INCYTE PHARMACEUTICALS, INC.
;      STREET:  3174 PORTER DRIVE
;      CITY:  PALO ALTO
;      STATE:  CALIFORNIA
;      COUNTRY:  USA
;      ZIP:  94304
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  Word Perfect 6.1 for Windows/MS-DOS 6.2
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/09/023,655
;      FILING DATE:  HEREWITH
;      CLASSIFICATION:
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:
;      FILING DATE:
;      CLASSIFICATION:
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Zeller, Karen J.
;      REGISTRATION NUMBER:  37,071
;      REFERENCE/DOCKET NUMBER:  PA-0001 US
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (650) 855-0555
;      TELEFAX:  (650) 845-4166
;  INFORMATION FOR SEQ ID NO:  1289:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  7680 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    IMMEDIATE SOURCE:
;      LIBRARY:  GENBANK
;      CLONE:  g31396
US-09-023-655-1289

  Query Match             81.2%;  Score 1743.4;  DB 4;  Length 7680;
  Best Local Similarity   97.0%;  Pred. No. 0;
  Matches 1805;  Conservative    0;  Mismatches   11;  Indels   45;  Gaps    1;

Qy        137 GAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGCCCCAGTCCCCGGTGGCTGTCAGTCA 196
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 GAAGAGCAAGAGGCAGGCTCAGCAAATGGTTCAGCCCCAGTCCCCGGTGGCTGTCAGTCA 60

Qy        197 AAGCAAGCCCGGTTGTTATGACAATGGAAAACACTATCAGATAAATCAACAGTGGGAGCG 256
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 AAGCAAGCCCGGTTGTTATGACAATGGAAAACACTATCAGATAAATCAACAGTGGGAGCG 120

Qy        257 GACCTACCTAGGCAATGCGTTGGTTTGTACTTGTTATGGAGGAAGCCGAGGTTTTAACTG 316
              |||||||||||| |||| ||||||||||||||||||||||||||||||||||||||||||||
Db        121 GACCTACCTAGGTAATGTGTTGGTTTGTACTTGTTATGGAGGAAGCCGAGGTTTTAACTG 180

Qy        317 CGAGAGTAAACCTGAAGCTGAAGAGACTTGCTTTGACAAGTACACTGGGAACACTTACCG 376
              ||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 CGAAAGTAAACCTGAAGCTGAAGAGACTTGCTTTGACAAGTACACTGGGAACACTTACCG 240

Qy        377 AGTGGGTGACACTTATGAGCGTCCTAAAGACTCCATGATCTGGGACTGTACCTGCATCGG 436
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AGTGGGTGACACTTATGAGCGTCCTAAAGACTCCATGATCTGGGACTGTACCTGCATCGG 300

Qy        437 GGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTGCCATGAAGGGGGTCAGTC 496
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTGCCATGAAGGGGGTCAGTC 360

Qy        497 CTACAAGATTGGTGACACCTGGAGGAGACCACATGAGACTGGTGGTTACATGTTAGAGTG 556
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 CTACAAGATTGGTGACACCTGGAGGAGACCACATGAGACTGGTGGTTACATGTTAGAGTG 420

Qy        557 TGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCTGCAAGCCCATAGCTGAGAAGTGTTT 616
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 TGTGTGTCTTGGTAATGGAAAAGGAGAATGGACCTGCAAGCCCATAGCTGAGAAGTGTTT 480

Qy        617 TGATCATGCTGCTGGGACTTCCTATGTGGTCGGAGAAACGTGGGAGAAGCCCTACCAAGG 676
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 TGATCATGCTGCTGGGACTTCCTATGTGGTCGGAGAAACGTGGGAGAAGCCCTACCAAGG 540

Qy        677 CTGGATGATGGTAGATTGTACTTGCCTGGGAGAAGGCAGCGGACGCATCACTTGCACTTC 736
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 CTGGATGATGGTAGATTGTACTTGCCTGGGAGAAGGCAGCGGACGCATCACTTGCACTTC 600

Qy        737 TAGAAATAGATGCAACGATCAGGACACAAGGACATCCTATAGAATTGGAGACACCTGGAG 796
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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